APOSTEL 2.0 Recommendations for Reporting Quantitative Optical Coherence Tomography Studies

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Abstract

Objective

To update the consensus recommendations for reporting of quantitative optical coherence tomography (OCT) study results, thus revising the previously published Advised Protocol for OCT Study Terminology and Elements (APOSTEL) recommendations.

Methods

To identify studies reporting quantitative OCT results, we performed a PubMed search for the terms "quantitative" and "optical coherence tomography" from 2015 to 2017. Corresponding

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Glossary

APOSTEL = Advised Protocol for OCT Study Terminology and Elements; **GRADE** = Grading of Recommendations Assessment, Development and Evaluation; **OCT** = optical coherence tomography; **OCT-A** = optical coherence tomography angiography.

authors of the identified publications were invited to provide feedback on the initial APOSTEL recommendations via online surveys following the principle of a modified Delphi method. The results were evaluated and discussed by a panel of experts and changes to the initial recommendations were proposed. A final survey was recirculated among the corresponding authors to obtain a majority vote on the proposed changes.

Results

A total of 116 authors participated in the surveys, resulting in 15 suggestions, of which 12 were finally accepted and incorporated into an updated 9-point checklist. We harmonized the nomenclature of the outer retinal layers, added the exact area of measurement to the description of volume scans, and suggested reporting device-specific features. We advised to address potential bias in manual segmentation or manual correction of segmentation errors. References to specific reporting guidelines and room light conditions were removed. The participants' consensus with the recommendations increased from 80% for the previous APOSTEL version to greater than 90%.

Conclusions

The modified Delphi method resulted in an expert-led guideline (evidence Class III; Grading of Recommendations, Assessment, Development and Evaluations [GRADE] criteria) concerning study protocol, acquisition device, acquisition settings, scanning protocol, funduscopic imaging, postacquisition data selection, postacquisition analysis, nomenclature and abbreviations, and statistical approach. It will be essential to update these recommendations to new research and practices regularly.

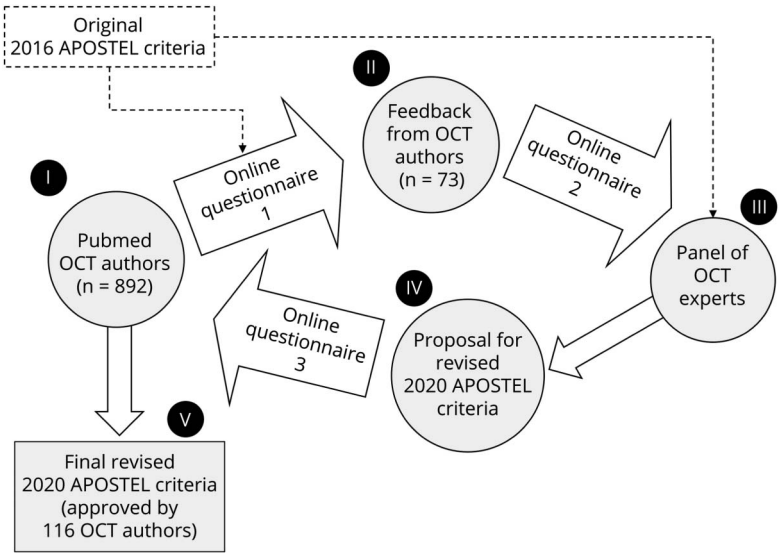
Increases in the numbers of quantitative optical coherence tomography (OCT) studies have raised the need for consistent and coherent standardized reporting recommendations. In 2016, the Advised Protocol for OCT Study Terminology and Elements (APOSTEL) recommendations were published to provide a 9-point checklist of relevant aspects for reporting quantitative retinal OCT studies.[1] The original APOSTEL recommendations were conceived as expert opinion (level D evidence according to the Grading of Recommendations Assessment, Development and Evaluation [GRADE] working group criteria; gradeworkinggroup.org) from discussions among the authors, the IMSVISUAL consortium (imsvisual.org), and consideration of the literature.[2] Without a formal consensus-building approach, and without involving a broader audience, further validation was warranted. We aimed to revise and achieve consensus on these recommendations by using a modified Delphi method, including a larger group of OCT scientists and clinicians, in a formal procedure to review the consensus and develop level C evidence-based guidelines (GRADE criteria).[3] The long-term goal was to improve the reproducibility and interoperability of OCT studies for retinal and neuro-ophthalmology diseases.

Methods

In order to identify experts in the field while minimizing the risk of selection bias, we chose to contact corresponding authors of studies reporting quantitative retinal OCT results published within 24 months prior to our initial survey by email. A total of 892 authors of 1,189 publications were identified by a PubMed search (performed 3 July 2017) using the search terms "quantitative" and "optical coherence tomography" for 2015 to 2017. The Delphi method is a systematic, multistage survey to obtain consensus on a specified question. The process involves multiple rounds of questionnaires presented to participants. The responses are analyzed by a panel of experts and fed back to participants and assessed for consensus.[4] Most of the members of the panel of experts were also corresponding authors of quantitative retinal OCT studies and were therefore also invited to participate in the survey. Following the consensus-building procedure of a modified Delphi method (figure 1), we conducted the following steps:

1. We contacted all corresponding authors of the identified publications and asked them to evaluate and give feedback on the initial APOSTEL recommendations. The participants were asked about their agreement on each item of the recommendations, rating from 1 (full disagreement) to 4 (full approval). Participants were given the opportunity to provide comments. In a blinded fashion, we collected feedback and suggestions using a free online survey via Google Forms (initial questionnaire; raw data of survey results can be obtained from the corresponding author upon qualified request).
2. We then formed a panel of 54 international experts who gathered at congress meetings and during 4 rounds of telephone conferences. The aggregated results of the initial questionnaire were reviewed online through a second questionnaire by the panel, who also revised the original APOSTEL recommendations and proposed a list of changes.

Figure 1 Modified Delphi Method



The modified Delphi method is described as a consensus-building process. We contacted 892 authors of quantitative (optical coherence tomography [OCT]) studies identified by PubMed (I) using an online survey, in which feedback on the original Advised Protocol for OCT Study Terminology and Elements (APOSTEL) 2016 criteria was requested. The feedback of the 73 responding OCT authors was analyzed by a panel of experts (II) and changes to the APOSTEL recommendations were proposed (III). A revised version (IV) was proposed to the OCT authors (n = 116), who approved the revisions by majority vote, which led to the final revised 2020 APOSTEL criteria (V).

3. This list was then reviewed in a second Delphi round by the original group of corresponding authors through a third online questionnaire (Google Forms). In this last Delphi round, the participants were given the opportunity to approve or reject the final list of suggestions of the panel of experts by majority vote.

Results

Initial Questionnaire: Survey About the Initial APOSTEL Recommendations Among Corresponding Authors

Seventy-three (8%) of the 892 contacted corresponding authors of quantitative OCT studies completed the first online questionnaire and provided feedback, the majority of these being ophthalmologists (71%), followed by neurologists (10%) and neuro-ophthalmologists (10%). Eighty percent of participants agreed with the recommendations as they were published and 95% planned to adhere to the recommendations in future publications. At the same time, 64% stated having reported their previous research with less detail than suggested.

Second Questionnaire: Consensus Building With the Panel of Experts

Based on the feedback obtained during the first survey, the panel of 54 experts drafted a list of 15 suggested changes to the original APOSTEL recommendations. Twelve (80%) of these suggestions (see below) were accepted through the second questionnaire, while proposals already covered in the original recommendations or to include OCT angiography (OCT-A) were rejected. With this feedback, we generated a revised version of the APOSTEL recommendations with an updated 9-point checklist.

Third Questionnaire: Second Delphi Round With Corresponding Authors

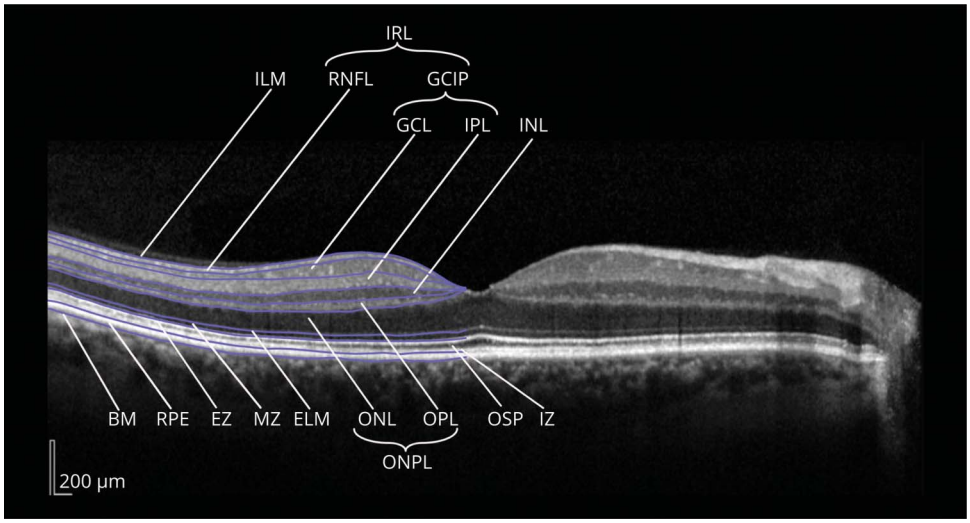
A total of 116 (13%) of the 892 corresponding authors responded to the third survey. Among them, 53% were ophthalmologists, 35% neurologists, and 12% non-MD researchers. The overall acceptance of the proposed changes was over 95%, with the only exception of the recommendation to report the pixel to millimeter ratio and the image format if the images are exported from the device for analysis, which was accepted by 84% of the authors.

Summary of Revisions

After the modified Delphi process for consensus building, we decided to maintain the initial recommendations of stating the acquisition protocol and imaging modalities and addressing concomitant eye pathologies with the exact scanning protocol. The changes made to the original APOSTEL recommendations checklist are highlighted in the table and summarized below:

1. As already addressed in correspondence to the initial recommendations,[5] we harmonized the nomenclature of the outer retinal layers to match the 2014 consensus article by Staurenghi et al.[6] (figure 2).
2. We removed references to specific reporting guidelines to avoid favoring any guidelines or omitting relevant recommendations.
3. When utilized, we suggest reporting device-specific features (e.g., enhanced depth imaging, swept-source OCT, adaptive optics).
4. We added the exact area of measurement (e.g., analysis grids) to the description of volume scans.
5. We added a commentary regarding the importance of addressing potential bias in manual segmentation or manual correction of segmentation errors (masking). In several comments, concerns were raised regarding the

Figure 2 Consensus Nomenclature for Retinal Structures



The different layers (and their boundaries) are illustrated in a central horizontal spectral-domain optical coherence tomography scan through the middle of the fovea. Retinal structures and layers: BM = Bruch membrane; ELM = external limiting membrane; EZ = ellipsoid zone (inner and outer segment junction); GCL = ganglion cell layer; ILM = inner limiting membrane; INL = inner nuclear layer; IPL = inner plexiform layer; IZ = interdigitation zone; MZ = myoid zone; ONL = outer nuclear layer; OPL = outer plexiform layer; OSP = outer segment of the photoreceptors; RNFL = retinal nerve fiber layer; RPE = retinal pigment epithelium. Compound layers: GCIP = ganglion cell and inner plexiform layer (composite of macular GCL and IPL); IRL = inner retinal layers (composite of macular RNFL, GCL, and IPL); ONPL = outer nuclear and plexiform layer (composite of ONL and OPL). Copyright by IMSVISUAL and licensed under CC-BY-4.0 for this publication (imsvisual.org/resources/media).

length of the methodology section of articles that fully adhered to the APOSTEL recommendations. In case of limited word count availability, we now advise submitting the exact OCT methodology as supplementary material, if permitted.

6. Another issue raised by several comments was concerning the relevance of some of the details to be reported regarding the acquisition setting, namely the room lighting conditions and whether pupils were dilated. The panel of experts agreed that reporting the ambient lighting condition is likely to be of low clinical importance, although shaded room lighting is suggested. However, off-axis beam placement could affect the results of OCT imaging studies, and the risk for this phenomenon increases with pupil dilation and is greater for the outer retinal layers (outer plexiform layer/outer nuclear layer) compared to the inner retinal layers (peripapillary retinal nerve fiber layer to inner nuclear layer).[7] Oberwahrenbrock and colleagues[8] showed that the greatest error is for the outer retinal layers. Therefore, pupil dilation is relevant because it can directly affect quantitative OCT measures. We thus omitted room light conditions but retained pupil dilation.

Discussion

The formal consensus-building approach of a modified Delphi method was used to revise the APOSTEL recommendations for the reporting of quantitative OCT studies.

We observed a high consensus of the participants already with the initial APOSTEL recommendations in the first survey. The majority of the participants acknowledged the need for guidance.

Whereas the original APOSTEL recommendations were conceived by a panel dominated by neurologists, a more heterogeneous mix of specialties, with broader expertise, contributed to this new version, the majority being ophthalmologists. Ninety-seven percent of all participants agreed that that the APOSTEL 2.0 guidelines should apply to all studies reporting on quantitative retinal OCT research and not be restrained to certain disorders or disciplines. Furthermore, choosing to identify the experts to be addressed by the survey as the corresponding authors of relevant research articles based on a PubMed search assured a broad consensus-building approach, eliminating the selection bias typically immanent to expert consortia. However, there was a low response rate[9]: 8% of the contacted corresponding authors responded to the first round of the survey and 13% to the second round. Possible explanations for this limitation may include the fact that corresponding authors are senior supervisors or principal investigators and are not necessarily as involved in the technical details and specifications addressed by the APOSTEL recommendations. Likewise, there are time constraints to consider. This can be viewed as a limitation of the study but we have to assume that those who participated in the survey were knowledgeable about the matter and contact details for the first authors or technicians involved in these studies were not available.

The modified Delphi method tends to eliminate extreme (but possibly relevant) positions and steers a middle-course consensus. However, all survey participants were given the opportunity to provide feedback in free text and all comments were critically discussed among the panel of experts. The achieved consensus is based on the opinion of the participants and the panel of experts and therefore it should be regularly counterchecked and revised along with evolving scientific evidence.

Table Nine-Point Advised Protocol for OCT Study Terminology and Elements (APOSTEL) Checklist (Adapted From Cruz-Herranz et al.[1])

Item	Category	Recommendation
1	Study protocol	(1) Describe how many OCT operating sites and graders were included (2) Report the timing of OCT compared to other measurements (same day, delayed) (3) Describe the inclusion and exclusion criteria (4) In case of limited word count, consider submitting the exact methodology as supplementary material[a]
2	Acquisition device	For all OCT devices used, report data on: (1) Manufacturer (2) Model (3) Version (4) Software version (5) Device type (time/spectral domain, swept-source, adaptive optics)[a]
3	Acquisition settings	Clearly describe the settings in which OCT scans were obtained: (1) Pupils dilated before examination (y/n) (2) Number of operators and devices[b]
4	Scanning protocol	Clearly describe the scanning protocol, including: (1) Type of scan (circular, volume, star, line, other) (2) Location (area of interest, macula, optic nerve head, papillomacular bundle, other) (3) Scan parameters (with or without eye tracking) Volume scan: size of scan, area and location of measurement (degrees or millimeters), number of B-scans, alignment of B-scans, number of A-scans per B-scan[a] Radial scan: size of scan area (degrees or millimeters), number of B-scans, alignment of B-scans, number of A-scans per B-scan Ring scan: diameter, A-scans/B-scan, manual or automatic placement of ring or method of centering, depth resolution Line scan: angle, location, number of A-scans, depth resolution
5	Funduscopic imaging	(1) Report other imaging modalities used in addition to OCT (funduscopy, confocal scanning laser ophthalmoscope, retinal angiography, autofluorescence imaging, etc.) (2) Describe acquisition protocol, including: Excitation wavelength Filter sets Number of frames averaged (if applicable) Report device specific features when utilized (e.g., enhanced depth imaging, swept-source OCT, adaptive optics)[a]
6	Postacquisition data selection	Describe image selection process, including: (1) Quality control criteria (2) Postacquisition discard (number and criteria) (3) Eye selection strategy (if applicable)
7	Postacquisition analysis	Describe all postacquisition steps: (1) Software used for processing scans and segmentation (may be different from acquisition software) (2) Which individual retinal layers were segmented/included (3) Method of segmentation (automated, semi-automated, or manual) (4) How potential bias was addressed in the case of manual segmentation or manual correction of automated segmentation errors (masking)[a] (5) Grid used for data extraction (size, shape, selected sections) (6) Pixel to millimeter ratio if images are exported (caliper need)[a]
8	Nomenclature and abbreviations	Define: (1) Anatomical structures analyzed (2) Units of provided measurements (e.g., volume or thickness) (3) Report the number of eyes presenting additional retinal pathology; describe qualitative retinal changes and report exact methodology of quantification[a]
9	Statistical approach	Describe: (1) Statistical models used for the analyses of OCT data (2) Whether data were analyzed by eye or by patient

Abbreviation: OCT = optical coherence tomography.
The modified APOSTEL checklist containing 9 important items when reporting quantitative OCT studies.
[a] Changes made to the original APOSTEL recommendations checklist.
[b] Room light conditions were removed.

These recommendations do not cover all aspects and techniques possibly amenable to OCT research and are based on expert opinion and a single consensus finding investigation rather than on a systematic review of a large body of literature. Therefore, they are not intended as an indispensable premise for all experimental OCT research. The APOSTEL recommendations are intended for clinical OCT studies using established techniques and help to provide the necessary comparability between studies.

Some additions suggested during the revision process were not included in the final version as consensus was not reached. One of these suggestions was to incorporate a section on OCT-A. However, the inclusion of details pertaining to OCT-

A in the APOSTEL 2.0 recommendations would be premature. The field of OCT-A, both clinically and academically, is in a phase of rapid evolution and essentially in its infancy. Its use is not well established in routine clinical care in either the fields of ophthalmology or neurology. Interpretation of OCT-A scans across devices is challenging and standardized quantitative OCT-A metrics are lacking or vary across OCT platforms. Moreover, there is a lack of consensus regarding quality control criteria for image acquisition and the implementation of such standards as they pertain to OCT-A. These limitations are likely to change in the future. For these reasons, the evidence and corresponding investigative and clinical recommendations for OCT and OCT-A should remain on separate tracks.

A future revision of the APOSTEL criteria likely will also need to consider the role of artificial intelligence–based data from image analyses.[10]

We present revised APOSTEL recommendations based on this investigation using a modified Delphi process that involves a broad group of experts. Therefore, the resulting APOSTEL 2.0 can be considered an expert-led guideline (evidence class C, GRADE criteria) covering all relevant aspects of quantitative retinal OCT research. It will be necessary to update these recommendations to new research and practices regularly.

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Sven Meuth received honoraria for lecturing and travel expenses for attending meetings from Almirall, Amicus Therapeutics Germany, Bayer Health Care, Biogen, Celgene, Diamed, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis, Novo Nordisk, ONO Pharma, Roche, Sanofi-Aventis, Chugai Pharma, QuintilesIMS, and Teva; and his research is funded by the German Ministry for Education and Research (BMBF), Deutsche Forschungsgemeinschaft (DFG), Else Kröner Fresenius Foundation, German Academic Exchange Service, Hertie Foundation, Interdisciplinary Center for Clinical Studies (IZKF) Muenster, German Foundation Neurology, and Almirall, Amicus Therapeutics Germany, Biogen, Diamed, Fresenius Medical Care, Genzyme, Merck Serono, Novartis, ONO Pharma, Roche, and Teva. Elena H. Martínez-Lapiscina is, since 16 April 2019, an employee of the European Medicines Agency (Human Medicines). 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Shiv Saidha has received consulting fees from Medical Logix for the development of CME programs in neurology and has served on scientific advisory boards for Biogen, Genzyme, Genentech Corporation, EMD Serono, and Celgene; is the PI of investigator-initiated studies funded by Genentech Corporation and Biogen Idec; received support from the Race to Erase MS foundation; was the site investigator of a trial sponsored by MedDay Pharmaceuticals; and has received equity compensation for consulting from JuneBrain LLC, a retinal imaging device developer. Sven Schippling reports no conflicts of interest. Joel S. Schuman reports the following: Aerie Pharmaceuticals, Inc., Ocular Therapeutix, Inc., Opticient: consultant/advisor, equity owner; Bright Focus

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Name	Location	Contribution
Aykut Aytulun, MD	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany	Study concept and design, acquisition of data, analysis and interpretation, drafting and critical revision of the manuscript for important intellectual content, took part in the panel discussions
Andrés Cruz-Herranz, MD, PhD	Department of Neurology, University of California San Francisco	Study concept and design, acquisition of data, analysis and interpretation, drafting and critical revision of the manuscript for important intellectual content, took part in the panel discussions
Orhan Aktas, MD	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Laura J. Balcer, MD	Departments of Neurology, Population Health, and Ophthalmology, NYU Grossman School of Medicine, New York, NY	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Lisanne J. Balk, PhD	Mulier Institute, Centre for Research on Sports in Society, Utrecht, the Netherlands	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Piero Barboni, MD	Scientific Institute San Raffaele, Milan, Italy	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Augusto Azuara Blanco, MD	Centre for Public Health, Queen's University Belfast, Northern Ireland, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Peter A. Calabresi, MD	Division of Neuroimmunology, Johns Hopkins University, Baltimore, MD	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Fiona Costello, MD	Departments of Clinical Neurosciences and Surgery, University of Calgary, Alberta, Canada	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Bernardo Sanchez-Dalmau, MD, PhD	Institut d'Investigacións Biomèdiques August Pi i Sunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Delia Cabrera DeBuc, PhD	Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, FL	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Nicolas Feltgen, MD	Department of Ophthalmology, University Medical Center, Göttingen, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions

Appendix *(continued)*

Name	Location	Contribution
Robert P. Finger, MD, PhD	Department of Ophthalmology, University of Bonn, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Jette Lautrup Frederiksen, MD, DMSci	Department of Neurology, Rigshospitalet Glostrup and University of Copenhagen, Denmark	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Elliot Frohman, MD	Laboratory of Neuroimmunology, Stanford University School of Medicine, CA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Teresa Frohman, MD	Laboratory of Neuroimmunology, Stanford University School of Medicine, CA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
David Garway-Heath, MD	Institute of Ophthalmology, University College London; Moorfields Eye Hospital NHS Foundation Trust, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Iñigo Gabilondo, MD, PhD	Biocruces Bizkaia Health Research Institute, Barakaldo, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Jennifer S. Graves, MD, PHD, MAS	Department of Neurosciences, University of California, San Diego	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Ari J. Green, MD	Department of Neurology, University of California San Francisco, CA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Hans-Peter Hartung, MD, FRCP	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany; Brain and Mind Centre, University of Sydney, Australia; Department of Neurology, Medical University of Vienna, Austria	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Joachim Havla, MD	Institute of Clinical Neuroimmunology, LMU Hospital, Ludwig-Maximilians Universität München, Munich, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Frank G. Holz, MD	Department of Ophthalmology, University of Bonn, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions

Appendix *(continued)*

Name	Location	Contribution
Jaime Imitola, MD	UConn Health Comprehensive MS Center, Division of Multiple Sclerosis and Neuroimmunology, Department of Neurology, University of Connecticut School of Medicine, Farmington	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Rachel Kenney, MPhil	Departments of Neurology, Population Health and Ophthalmology, NYU Grossman School of Medicine, New York, NY	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Alexander Klistorner, PhD	Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Benjamin Knier, MD	Department of Neurology, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Thomas Korn, MD	Department of Neurology, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Scott Kolbe, MD	Department of Medicine and Radiology, University of Melbourne, Australia	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Julia Krämer, MD	Department of Neurology with Institute of Translational Neurology, University of Münster, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Wolf A. Lagrèze, MD	Eye Center, Medical Center, Faculty of Medicine, University of Freiburg, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Letizia Leocani, MD, PhD	Experimental Neurophysiology Unit, Institute of Experimental Neurology (INSPE), IRCCS San Raffaele, University Vita-Salute San Raffaele, Milan, Italy	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Oliver Maier, MD	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions

Continued

Appendix *(continued)*

Name	Location	Contribution
Elena H. Martínez-Lapiscina, MD	Institut d'Investigacións Biomediques August Pi i Sunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Sven Meuth, MD	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Olivier Outteryck, MD	Univ. Lille, Inserm, CHU Lille, U1172-LilNCog (JPARC)-Lille Neurosciences & Cognition, France	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Friedemann Paul, MD	Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Axel Petzold, MD, PhD, FRCP	Moorfields Eye Hospital, The National Hospital for Neurology and Neurosurgery, Queen Square, UCL Institute of Neurology, London, UK; Neuro-ophthalmology Expert Center, Amsterdam UMC, the Netherlands	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Gorm Pihl-Jensen, MD	Department of Neurology, Rigshospitalet Glostrup and University of Copenhagen, Denmark	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Jana Lizrova Preiningerova, MD, PhD	Department of Neurology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Gema Rebolleda, MD, PhD	Department of Ophthalmology, Ramon y Cajal Hospital, Medicine University of Alcalá, Madrid, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Marius Ringelstein, MD	Department of Neurology, Center for Neurology and Neuropsychiatry, LVR-Klinikum, Heinrich-Heine-University Düsseldorf, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Shiv Saidha, MD	Division of Neuroimmunology, Johns Hopkins University, Baltimore, MD	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Sven Schippling, MD	Department of Neurology, University Hospital Zurich, Switzerland	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Joel S. Schuman, MD	Departments of Neurology, Population Health and Ophthalmology, NYU Grossman School of Medicine, New York, NY	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Robert C. Sergott, MD	Thomas Jefferson University Medical College, Philadelphia, PA	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Ahmed Toosy, MD	Queen Square MS Centre, Department of Neuroinflammation, UCL Institute of Neurology, University College London, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Pablo Villoslada, MD	Institut d'Investigacións Biomediques August Pi i Sunyer (IDIBAPS) and Hospital Clinic, University of Barcelona, Barcelona, Spain	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Sebastian Wolf, MD	Department of Ophthalmology and Department of Clinical Research, Bern University Hospital, University of Bern, Switzerland	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
E. Ann Yeh, MD	Division of Neurology, Department of Pediatrics, Hospital for Sick Children, Division of Neurosciences and Mental Health SickKids Research Institute, University of Toronto, Canada	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Patrick Yu-Wai-Man, PhD, FRCOphth, FRCPath	Department of Clinical Neurosciences, University of Cambridge; Moorfields Eye Hospital, London, UK	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Hanna G. Zimmermann, PhD	Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany	Analysis and interpretation, critical revision of the manuscript for important intellectual content, took part in the panel discussions
Alexander U. Brandt, MD	Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Germany; University of California, Irvine	Analysis and interpretation, study concept and design, acquisition of data, drafting and critical revision of the manuscript for important intellectual content, study supervision, took part in the panel discussions

Appendix *(continued)*

Name	Location	Contribution
Philipp Albrecht, MD	Department of Neurology, Medical Faculty, Heinrich-Heine University Düsseldorf, Germany	Analysis and interpretation, study concept and design, acquisition of data, drafting and critical revision of the manuscript for important intellectual content, study supervision, took part in the panel discussions

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